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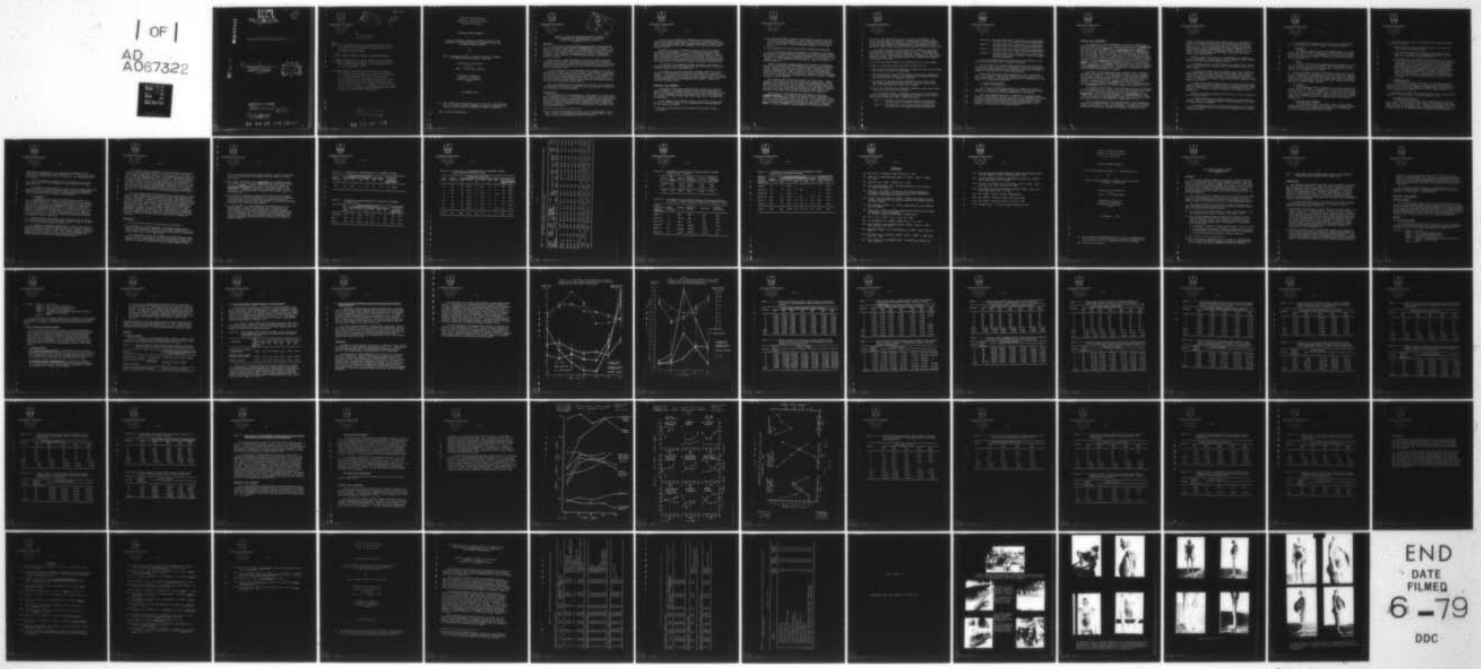

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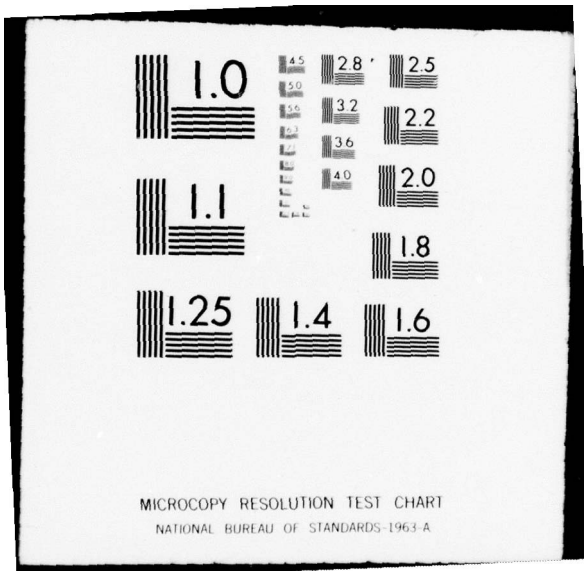
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SCHISTOSOMIASIS RESEARCH PROJECT
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Faculty of Medicine
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CONTENTS:

(1) EFFECT OF NUTRITION AND SOCIO-ECONOMIC STATUS ON THE PREVALENCE OF SCHISTOSOMIASIS IN AL-KHADRA VILLAGE & AL-KHADRA PRIMARY SCHOOL,

(2) THE ALTERED HORMONAL BALANCE IN SCHISTOSOMIASIS,

(3) MULTIPLE MEASURES OF CARDIAC OUTPUT BY THERMODILUTION DURING MITRAL COMMISSUROTOMY, LEFT VENTRICULAR AND CORONARY ANGIOGRAPHY, and

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TECHNICAL REPORT NUMBER I

EFFECT OF NUTRITION AND SOCIO-ECONOMIC STATUS ON THE PREVALENCE OF SCHISTOSOMIASIS IN AL-KHADRA VILLAGE AND AL-KHADRA PRIMARY SCHOOL ★

By

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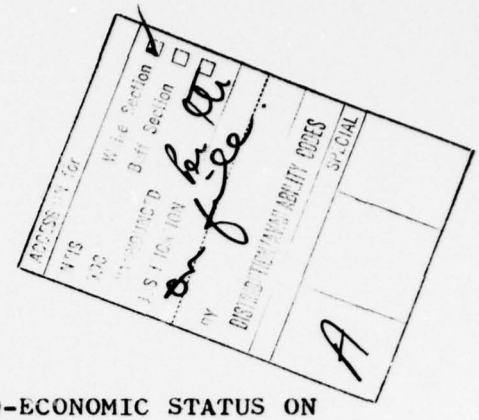

EFFECT OF NUTRITION AND SOCIO-ECONOMIC STATUS ON THE PREVALENCE OF SCHISTOSOMIASIS IN AL-KHADRA VILLAGE AND AL-KHADRA PRIMARY SCHOOL ★

ABSTRACT :

The prevalence of schistosomiasis in Al-Khadra primary school children was much higher compared with the adult population of Al-Khadra village. The peak of prevalence of schistosomiasis was noticed in the age group of 7-9 years, which is the most dynamic sector of the population. This could be considered as an index of a perpetual increase in the incidence of schistosomiasis among inhabitants of this rural area.

Total caloric intake and animal proteins were found seriously diminished in low income categories of the population. Anaemias, Ariboflavinosis, and to some extent pellagra and vitamin A deficiency were the other main nutritional,or partly nutritional,disorders in Al-Khadra primary school.

A high prevalence of schistosomiasis was encountered in lower income groups. Inspite of the major role of the effect of environmental factors on the prevalence of schistosomiasis, other factors such as nutrition and socio-economic status must also be considered viz : the prevalence of schistosomiasis was found to correlate with the low total caloric intake and the seriously deficient animal proteins in the diet of these low income groups.

The data obtained from the present survey point to the importance of considering the effect of Nutrition and Socio-economic Status on the prevalence of schistosomiasis.

INTRODUCTION :

The prevalence of schistosomiasis is the result of a rather complex ecological set up. It involves man, primarily, as the definitive host, accordingly its prevalence will be affected by the human aggregate and the percentage of individuals harboring mature worms and excreting viable and hatchable eggs. Likewise specific human activities are needed to allow for the contamination of fresh water with schistosomiasis eggs.

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The effect of nutrition on immunological reactivity is of great public health significance. There are indications that protein-energy deficiencies affect immune competence at various levels, thus rendering the human body vulnerable to infections and infestations (1,2,3).

Moreover, nutrition constitute a major role in the biology of growth and development. It is a well established fact that nutritional deficiency in pregnant and lactating mothers, infants and young children represents a major and urgent health problem in most developing countries. There is considerable evidence to indicate that all the basic characteristics of growth and development, are significantly influenced by protein and energy deficiencies(4).

In addition, developmental process occuring in the brain at different regions and in different ways may be affected by the nutritional status of the individuals(5).

The effect of nutrition and socio-economic status on the prevalence of schistosomiasis constitute two potentially important factors. Therefore the objectives of this study are mainly directed towards investigating the interrelationship between these two factors and the prevalence of schistosomiasis in Al-Khadra village and Al-Khadra primary school.

MATERIALS AND METHODS :

Al-Khadra village and Al-Khadra primary school were selected for this survey. Al-Khadra village lies at the northern part of Beheira Governorate, situated on the eastern bank of Mahmoudia canal, 12 km from Alexandria on the paved main road which lies alongside the canal. The rural health unit of the area lies at one km north of Al-Khadra.

This community would afford suitable conditions for the study of the role of the canals in the transmission of schistosomiasis for the following reasons :

1) The area is surrounded and traversed by a variety of water channels.

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2) The area was neither included in the Egypt-49 project; nor was it surveyed by the Ministry of Public Health snail control section. So the water channels offered a natural ecologic set up for the perpetuation of the schistosoma parasite in the snail vector.

3) The accessibility of this area gives an additional advantage.

A cross-sectional survey was conducted to determine the overall prevalence of schistosomiasis, nutritional and socio-economic status in Al-Khadra village. The information presented in this survey was obtained by random sampling technique; 73% of the total houses of the village (i.e. 919 individuals) were selected, using the table of random number (6).

Pupils of Al-Khadra primary school were examined to determine the overall prevalence of schistosomiasis and nutritional disorders. School children were chosen for being an easily accessible group lending themselves more readily than any other social aggregate to repeated examinations. Thus, the study of school children would yield highly reliable data concerning the prevalence of schistosomiasis as well as assessement of nutritional status in respect to income category of their families.

Urine samples were collected in large test tubes with a tapering end, that served both for collection and sedimentation. Stool samples were collected in 150 ml. capacity covered waxed paper cups. Containers were labelled, and the number of each container was written in tables next to the name of the subject investigated. Villagers and pupils were instructed to void stools and urine early in the morning of the next visit day and the samples were collected.

Enumeration of the population was carried out, using the canvasser approach. All individuals were recorded in household registry, with information about the members of the household, their relation to the household head, age and sex. This survey was carried out, systematically visiting each family at home, where their total diet per month and income were investigated according to special forms. We have relied to a large extent on the values declared by

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the head of the family and his wife being the housekeeper. The ration card was used as a monitor. Possession of cultivated land, cattle breeding and dairy products, and such activities as breeding of poultry, were taken into consideration. The products of such resources added certain portions to the families income and nutrition.

In respect of income, we have met with a difficult task while endeavouring to collect accurate data, as most of individuals have not been able to furnish us with definite figures. Great care has been taken to put them objective questions, recording all the answers regarding income. Our estimations have been conducted according to the following criteria :

1) The rent per acre (feddan) on an average is 20 L.E. per annum.

2) The net income per feddan per annum is about 50 L.E.

3) The price of food stuffs stored and consumed all over the year has been counted in terms of cash money.

4) The daily wages of agricultural labourers has been calculated on the official bases, which is 40 PT/day and the expected working days per year for the seasonal labourers.

5) The income of non-agricultural occupations, such as building labourers, mechanicians and drivers of tractors, brick layers, etc., has been based on a wage of 70 PT/day.

6) As for the officials and industrial labourers, they receive fixed salaries and can give real figures.

In this present survey, individuals and pupils of the primary school belonging to Al-Khadra village were divided into the following groups according to their income categories :

group I : includes those with a main source of income ranging from 12 to 7.5 Egyptian pounds/capita/month.

group II : includes those with a main source of income ranging from 7.49 to 6 Egyptian pounds/capita/month.

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group III : includes those with a main source of income ranging from 5.99 to 4.5 Egyptian pounds/capita/month.

group IV : includes those with a main source of income ranging from 4.49 to 3 Egyptian pounds/capita/month.

group V : includes those with a main source of income ranging from 2.99 to 1.5 Egyptian pounds/capita/month.

group VI : includes those with a main source of income ranging from 1.49 to zero (living on charity) Egyptian pounds/capita/month.

Within Al-Khadra village the population was homogenous with regard to social conditions, religion, and habits.

Current reports of vitamin deficiencies rely almost entirely on physical signs, inspite of the problems of observer variation(7). A thorough clinical examination of school children was performed in respect of the presence of vitamin deficiencies.

Fresh stool specimens were transported to the rural health unit, where immediate microscopic examinations were carried out by our trained staff . Results were recorded after examination of the stools by the following techniques :

1. direct foecal smear.
2. gravity sedimentation.

The finding of schistosoma eggs in the smears was taken as positive. Stools were considered negative if eggs were not detected on three repeated successive examinations of subjects.

The urine samples were left to sediment in collecting tubes and with a long pasteur pipette two drops of the sediment were transferred to microscope slide and examined. Negative samples were re-examined after centrifugation by a manual centrifuge. If eggs were not detected after three consecutive examinations of the patients, the urine were considered negative.

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RESULTS AND DISCUSSION :

The prevalence of schistosomiasis for the 919 villagers surveyed is shown in table 1. The overall prevalence of S. haematobium was 33.8% and for S. mansoni the corresponding figure was 3.7%. Evidence of infection with both S. haematobium and S. mansoni did not exceed 1.1%. Moreover, the overall prevalence of schistosomiasis in Al-Khadra village was 38.6%. The most striking finding was the insignificant shift in the prevalence of schistosomiasis infection since former studies in Al-Khadra area (8). Previous reports (9,10)in the Nile Delta and Qalyub region indicated also the higher prevalence of S. haematobium as compared with the prevalence of S. mansoni. However, Qalyub schistosomiasis project (11) reported higher prevalence of S. mansoni infection and a much lower prevalence of S. haematobium in Qalyub area. Differences in population samples, parasitological techniques and environmental factors hinder comparison between these published surveys.

Prevalence of schistosomiasis among primary school children of Al-Khadra (242 pupils) was categorized according to their village of residence (table 2). The prevalence of schistosoma haematobium among school children residing at Deif village was 67.5%, whereas in those living in Al-Khadra, it was relatively lower (57.4%). However, the prevalence of S. mansoni was slightly higher in Al-Khadra (9.7%) compared with Deif (6.4%). Such a high prevalance of S. haematobium has been previously reported in this area (8).

The school children from 7 to 9 years had the peak of prevalence of schistosomiasis, i.e., 84.6%, 91.7% and 76.9% respectively (table 3). A similar prevalence pattern has been also observed in S. haematobium. Moreover, the prevalence of S. haematobium was much higher than that of schistosoma mansoni in each year of age. Such a high prevalence of schistosomiasis among school children has been previously reported in the Egypt-49 project area (12).

These findings denote, that the prevalence of schistosomiasis among school children could be considered as an index of the transmission capabilities of the water channels. In addition the high prevalence of infection depends on geographic and agricultural

nature, as well as shallow canals passing close to the houses encouraging children to spend their time swimming and playing in water (13). Besides, this age group (7-9 years) is the most dynamic sector of the population and becomes independent earlier than children in the corresponding age group in urban areas. Though most children receive treatment, either complete or incomplete, on entering primary school, their activities and habits expose them to re-infection.

However, there is no reason to overemphasize the importance of the environmental factors and to ignore completely other factors such as nutrition and socio-economic status.

The pattern of diet in the village of Al-Khadra (1247 individuals) was determined as compared to the food balance sheet of the whole country.

In Al-Khadra village the diet provides the average individual with a mean value of total caloric intake of 2898 Kcal (table 4). According to this estimate, the diet in Al-Khadra village falls within the pattern of countries of low socio-economic status (i.e., 93% of the daily caloric intake comes from foods of vegetable origin, especially cereals).

Cereals alone provide villagers with the majority of the daily caloric intake, protein, thiamin, niacin, iron and riboflavin. This shows the importance of the type of cereals consumed and its extraction rate, in respect of their influence on the health of the population.

From the present field survey and tables (4,5 & 6) we conclude the following results :

1) Animal proteins are seriously deficient in low income categories. Most of the families depend on fish consumption, as being a cheeper source of protein.

2) Consumption of milk and its products depends on the possession of cows and duration of the period of milking, which is about 6 months per year.

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3) Carbohydrates constitute the main part of farmers' diet, i.e., bread and rice, as being cheaper than protein sources.

4) Calcium :

The WHO/FAO committee on calcium requirements (14) suggested that the practical allowance for adults should be between 400 and 500 mg. per day. In Al-Khadra the calcium intake reached the values given by the WHO/FAO committee i.e. from 406-737 mg/ daily. (see table 4).

5) Iron :

This diet provides the recommended daily allowance of iron, but 70% of this iron is from cereals. This complex with rural effect and blood loss caused by the burden of parasites will certainly lead to prevalence of anaemia.

Among the school children of Al-Khadra village who were clinically investigated the prevalence of anaemia was 57.5%, whereas in Deif village its prevalence was higher i.e. 76.8% (see table 5). This could be explained by the fact, that prevalence of schistosomiasis in Al-Khadra school children was lower compared with those belonging to Deif village (table 2).

6) Thiamin :

The recommended intake according to the joint committee of FAO/WHO (14) is 1.6 mgm. In Al-Khadra it exceeds this value, being 2.2 mgm (Table 4). It is evidently due to eating mainly carbohydrate diet, rich in thiamin, namely wheat, maize, rice and in addition other ingredients of foods. Signs of deficiency were totally absent in the school children of Al-Khadra even in low income categories.

7) Nicotinic acid (Niacin)

Our calculated intake of nicotinic acid in the various income categories are shown in table (4). The recommended intake according to the joint committee of FAO/WHO (14) is 6.6 mgm nicotinic acid equivalent/100 Kcal in diet.

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Regarding the diet habits in Al-Khadra, the following should be taken into account :

a. Bread is mixed of maize and wheat flour. The maize part constitutes at least one third.

b. As it is well known that nicotinic acid content of the maize part is bound in an inabsorbable term and therefore maize is a poor source of nicotinic acid.

c. Foods which are rich sources of nicotinic acid and tryptophane (Beef and eggs) are not eaten in sufficient quantities, or frequently, to meet the daily need of the human body, therefore pellagra is still met with; but the percentage has greatly been reduced as compared to previous years. Table (5) depicts the percentage of school children encountered suffering from pellegra. Moreover, pellagra was mainly encountered more in the low income categories as seen from the table (6). Examination of school children related to these income groups amounted to 11 out of 134, i.e. 8.2%.

8) Riboflavin (B_2) :

The calculated intake of the diet of each group mentioned in the table (4) vary according to income and quantity of foods consumed. The three last categories consume diets containing riboflavin below the level recommended by FAO/WHO expert group (14), i.e. 0.55/1000 Kcal in diet.

Examination of school children belonging to these income groups amounted to 52 out of 134, i.e., 38.8% (table 5 & 6).

9) Ascorbic Acid (Vit. C) :

The USA Food and Nutrition Board recommended that an adult male should receive the much larger amount of 75 mg/day. They have now reduced it to 60 mg/day (15). British authorities still think this is excessive and unnecessary. The League of Nations (16) recommendation of 30 mgm/day, received support from the results of

the Sheffield experiment (17), and has been endorsed by the Department of Health and Social Security (18). This is certainly not enough to maintain the body in a state of full saturation with the vitamin.

The intake range of ascorbic acid as calculated by us, has been found to be 56 - 104.2 mgm with a mean value of 73.23 mgm (see table 4).

The population investigated by us were mainly farmers, agrarians & partly industrial labourers who have ample sources of vegetables and fruits. No signs of Vitamin C deficiency was met among the school children who were clinically investigated.

10) Vitamin A :

According to the report of FAO/WHO Expert group (14), the recommended intake of adults of both sexes is 750 ug retinal per day (i.e. 2500 I.U.). For infants 0-6 months it is accepted that breast feeding by well nourished mothers is the best way to satisfy the nutritional requirements for vitamin A, while 6-12 months the requirements are 300 ug (i.e.990 IU) while from 1 to 3 years it is stated by the same group to be 250 ug (i.e. 830 IU), 4-6 years 300 ug (i.e. 990 IU), 7-9 years 400 ug (i.e. 1898 IU), 13-15 years 725 ug (i.e. 2392 IU) and 16-19 years boys and girls and adults 750 ug(i.e. 2500 IU).

According to the same report, data collected from 76 population groups recorded for the Near East an intake range of 400-4000 I.U., while an intake majority 500-2000 I.U.

Our results in Al-Khadra village gave a range of 974-2153 IU, varying according to income category (table 4). Serious Vitamin A deficiencies were absent, but the eyes of 3 male pupils (2.2%) were found affected with Bitot's Spots. The affected belonged to the categories of low income with an intake range of 974-1034 IU Xeropthalmia was not met with among school children.

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The highest overall prevalence of schistosomiasis was encountered in the low income group IV, V and VI i.e. 37.6, 36.6 and 48.4 percent respectively (table 7). The same pattern was observed for schistosoma haematobium, where the highest prevalence was met with in the low income groups (IV, V and VI). This high prevalence of schistosomiasis in the low income groups of the population of Al-Khadra village could be well correlated with the low total caloric intake found in these corresponding categories (table 4 and 7). The seriously deficient animal proteins in the diet of the low income groups of Al-Khadra villagers could also add to the explanation for this high prevalence of schistosomiasis among them (table 4 and 7).

The close association of malnutrition and infection constitutes a major public health problem is slowly becoming more apparent than before. The results of our present survey could demonstrate this inter-relationship of nutrition, socio-economic states and prevalence of schistosomiasis. Support for this view comes from reports of WHO Study Group on Diarrheal Disease (19) and WHO expert committee on Enteric Infections (20). A WHO Expert committee on Helminthiasis recommended a study of the nutritional factors involved in host resistance to heminth infections (21). Furthermore, the joint FAO/ WHO Expert committee on Nutrition (22) supported these recommendations and asked that WHO encourages further epidemiological studies on the interaction of malnutrition and infection in developing countries.

CONCLUSIONS :

From the present data we can conclude the following :

1) The prevalence of schistosomiasis in Al-Khadra primary school children was much higher than that of the adult population of the same village. This is a striking finding which must be considered among inhabitants of this rural area.

This perpetual rise in the incidence of schistosomiasis among this age group is expected in all rural areas with a similar ecological set up. This finding calls for an immediate attention to improve the present unfavourable rural ecology inorder to save

the young age group from the present higher incidence which will lead to a future higher prevalence than the present, as they grow older.

2) The overall prevalence of S. haematobium in Al-Khadra village and primary school was much higher than the corresponding figures for S. mansoni. However, infection with both types (S. haematobium and mansoni) affected a very small sector of the population. Moreover, there was no significant shift in the prevalence of schistosomiasis infection since former studies in Al-Khadra area.

3) Total caloric intake and animal proteins were found seriously diminished in low income categories of the population. Aneamias, Ariboflavinosis, and to some extent pellagra and vitamin A deficiency were the other main nutritional, or partly nutritional, disorders in Al-Khadra primary school.

4) A high prevalence of schistosomiasis was encountered in low income groups. Inspite of the major role of the effect of environmental factors on the prevalence of schistosomiasis, other factors such as nutrition and socio-economic status must also be considered viz : the prevalence of schistosomiasis was found to correlate with the low total caloric intake and the seriously deficient animal proteins in the diet of these low income groups.

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Table (1) : Prevalence of schistosomiasis in Al-Khadra village

Number examined	Persons infected with						Prevalence of schistosomiasis	
	S. haematobium		S. mansoni		Both types			
	No.	%	No.	%	No.	%	No.	%
919	311	33.8	34	3.7	10	1.1	55	38.6

Table (2) : Prevalence of schistosomiasis in pupils of Al-Khadra primary school.

	No. examined	Pupils infected with						Prevalence of schistosomiasis	
		S. haemtobium		S. mansoni		Both types			
		No.	%	No.	%	No.	%	No.	%
Al-Khadra	134	77	57.4	13	9.7	3	2.2	93	69.4
Deif	108	73	67.5	7	6.4	2	1.8	82	75.9
Total	242	150	62.0	20	8.3	5	2.0	175	72.3

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Table (3) : Prevalence of schistosomiasis in Al-Khadra primary school grouped according to age.

Age (years)	Number examined	Persons infected with							
		S.heamatobium		S. mansoni		Both types		Prevalence of schistosomiasis	
		No.	%	No.	%	No.	%	No.	%
6-	34	18	52.9	2	5.9	0	0	20	58.8
7-	65	50	76.9	3	4.6	2	3	55	84.6
8-	36	26	72.2	5	13.8	2	5.5	33	91.7
9-	13	8	61.5	2	15.4	0	0	10	76.9
10-	43	23	53.5	1	2.3	0	0	24	55.8
11-	23	13	56.5	4	17.4	0	0	17	73.9
12-	28	12	42.8	3	10.7	1	3.6	16	57.1
Total	242	150	62.0	20	8.3	5	2	175	72.3

Table (4) : Assessement of dietetic pattern in Al-Khadra village categorized according to income per capita per month in Egyptian Pounds.

Income categories capita/ month/L.E.	No.of individuals	Total caloric intake	Protein			Fats	Carbohydrates	Calsium	Iron	Thiamin	Niacin	Riboflavin	Ascorbic Acid	Vitamin A
			Total (gm)	Animal protein gm	Animal protein %	(gm)	(gm)	(mg)	(mg)	(mg)	(mg)	(mg)	(mg)	(I.U.)
group I	21	3258	108.5	40.5	37.3	68.9	556.5	737	32.28	2.56	22.10	1.63	104.2	2153.5
group II	62	3394	102.0	30.0	29.4	64.0	617.0	501	32. 1	2.45	22.85	1.39	72.2	1478.0
group III	26	3007	90.0	21.0	23.3	61.0	536.0	523	30.92	2.36	18.91	1.28	94.1	1555.0
group IV	234	2752	80.0	18.0	22.5	53.8	502.0	406	27.59	2.11	16.18	1.15	56.0	1026.0
group V	577	2549	70.0	12.0	17.1	55.0	462.0	409	27.16	1.89	14.44	1.04	56.6	974.0
group VI	327	2428	66.0	10.0	15.1	47.0	452.0	415	24.17	1.86	14.00	1.04	56.3	1034.0
Total	1247	17388	516.5	131.5	144.7	349.7	3125.5	2991	174.43	13.32	108.48	7.53	439.4	8220.5
Mean		2898	86.08	21.91	24.11	58.28	520.9	498.5	29.07	2.2	18.08	1.25	73.23	1370.08

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Table (5) : Prevalence of Nutritional diseases among Al-Khadra primary school children.

Village	No. Examined	Anaemia	Aribof-lavinosis	Pellagra	Vitamin A deficicncy
Al-Khadra	134	57.5%	38.8%	8.2%	2.2%
Deif	108	76.8%	60.0%	12.0%	0.9%
Total	242	66%	48%	9.9%	1.6%

Table (6) : Prevalence of nutritional diseases categorized according to income in school children residing in Al-Khadra village.

Income categories capita/ month/L.E.	Number Examined	Anaemia	Aribofla-vinosis	Pellagra	Vitamin A dificiency
group I	1	NIL	NIL	NIL	NIL
group II	6	16.7%	NIL	NIL	NIL
group III	2	50%	NIL	NIL	NIL
group IV	28	64.3%	46.4%	3.6%	NIL
group V	57	52.6%	38.6%	8.8%	1.7%
group VI	40	67.5%	42.5%	12.5%	5%

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Table (7) : Prevalence of schistosomiasis in Al-Khadra village categorized according to income.

Income category (capita/ month/L.E.)	Number Examined	Persons infected with S.haematobium		S.mansoni		Both types		Prevalence of schistosomiasis	
		No.	%	No.	%	No.	%	No.	%
Group I	15	3	20.0	-	-	-	-	3	20.0
Group II	39	7	17.9	2	5.1	-	-	9	23.0
Group III	26	7	26.9	-	-	-	-	7	26.9
Group IV	178	57	32.0	7	3.9	3	1.7	67	37.6
Group V	434	143	32.9	12	2.8	4	0.9	159	36.6
Group VI	227	94	41.4	13	5.7	3	1.3	110	48.4
Total	919	311	33.8	34	3.7	10	1.1	355	38.6

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TECHNICAL REPORT NUMBER II

THE ALTERED HORMONAL BALANCE IN SCHISTOSOMIASIS ★

By

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THE ALTERED HORMONAL BALANCE IN SCHISTOSOMIASIS ★

ABSTRACT :

The delicate balance between the anterior pituitary hormones and their interaction with the other hormones indicates that the study of any altered hormonal balance must be done as a whole and not be limited to any single hormone. The present work is a study of human growth hormone, corticotrophin and cortisol blood levels and their role in hindering growth and development in endemic schistosomiasis with and without infantilism as compared with that of normal subjects.

The objective of the present study is to investigate the blood levels of these hormones at rest and their response to stress in patients with schistosomiasis with and without infantilism and normal controls of the same age group by radioimmunoassay methods.

The data obtained from this patient group as compared with that from normal control subjects from the same age group indicate the following altered hormonal balance :

A) The resting fasting blood levels of human growth hormone, corticortrophin and cortisol are within the normal range.

B) The following blood levels of human growth hormone, corticotriphin and cortisol levels are altered during glucose and insulin tolerance tests. Their deviations from the normal response are more marked when schistosomiasis is associated with infantilism :

1. A paradoxic response of human growth hormone to oral glucose.
2. An inadequate and delayed response of human growth hormone, corticotriphin and cortisol to insulin induced hypoglycemia.
3. Insulin-resistance and impaired glucose tolerance.

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PART I : SERUM HUMAN GROWTH HORMONE (HGH) LEVELS IN HEPATOSPLENIC SCHISTOSOMIASIS WITH AND WITHOUT INFANTILISM.

INTRODUCTION :

The lesions and syndromes resulting from schistosomal infection are numerous and appear not to spare any single organ in the human body including the endocrine system. Clinical observations have shown interference with growth and sexual development in cases of chronic schistosomiasis (1,2). However, assessement of pituitary function in schistosomiasis has been hindered by technical difficulties in assay of its hormones. The recent progress and availability of radioimmunoassay techniques have now made this investigation feasible and more accurate.

The current available data on circulating human growth hormone levels indicate that the production of this hormone should be determined from two points of view (3) :

1) Suppression of HGH levels to values found at the lower end of the normal range must be demonstrated to exclude excessive growth hormone secretion. In this connection, cirrhosis due to primary liver disease is associated with raised fasting plasma HGH levels that often do not fall after glucose loading; indeed paradoxical rises are sometimes seen (4,5). Similar findings were reported in chronic active hepatitis (6); the degree of HGH rise being related to the severity of the hepatitis. Furthermore, human growth hormone levels were found to be elevated and non suppressible in mal-nutrition states such as anorexia nervosa (7), Kwashiorker (8) and Marasmus (9).

2) Stimulation tests to obtain high normal values are necessary to exclude hypopituitarism. Low levels of human growth hormone are often found in normal people simulating hypopituitarism. It is therefore necessary to study the response of the patient's plasma human growth hormone level to stressful situations that normally produce a significant increase in this hormone levels before the

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diagnosis of hypopituitarism can be made in terms of human growth hormone secretion (3). Failure of human growth hormone levels to rise following insulin-induced hypoglycemia has been reported in cases of Haemochromatosis (10), Cystic fibrosis (11), Lipoatrophic diabetes (4,5) and in "emotional deprivation dwarrism" (12).

The aim of the present study is to assess the role of the anterior pituitary gland in hindering normal growth and sexual development in hepatosplenic schistosomiasis.

MATERIALS AND METHODS :

Subjects Studied :

Eight male patients (mean age 14 ± 1.5) with established diagnosis of chronic hepatosplenic schistosomiasis and clinical evidence of stunted growth and infantilism were compared with six male patients of the same age group and socio-economic status, with hepatosplenic schistosomiasis but without clinical evidence of retardation of growth or sexual development. Both groups were also compared against six normal controls of matched age and socio-economic conditions.

Methods : -

a) The Clinical Study :

All patients were subjected to a thorough clinical examination in which the size of the liver and spleen was recorded and graded according to the level of the lower border as follows (13) :

1. Liver : Grade 0 : not felt.
Grade 1 : felt on deep inspiration.
Grade 2 : felt below the costal margin.
Grade 3 : reaching the umbilicus.
Grade 4 : reaching a line drawn between both superior anterior iliac spines.
Grade 5 : more.

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2. Spleen : Grade 0 : not felt.
Grade 1 : felt on deep inspiration.
Grade 2 : felt below the costal margin.
Grade 3 : reaching the umbilicus.
Grade 4 : reaching a line drawn between both superior anterior iliac spines.
Grade 5 : more.

All subjects were screened clinically for evidence of nutritional deficiences or ascites. Patients with manifestations of nutritional deficiencies or moderate to severe ascites were excluded from the study.

b) Basic Laboratory Investigations :

Liver function tests (serum bilirubin, Alkaline Phosphatase, SGOT, SGPT, Total proteins, serum albumen, globulin and prothrombin time)were performed in addition to routine hematological investigation. Inorder to validate schistosomiasis infection, urine and stools examination for schistosomal eggs and other parasites were performed as well as intradermal test for schistosomiasis and rectal swabs. Percutaneous liver biopsies were also performed to confirm the schistosomal origin of the hepatic lesion.

c) Hormonal Assays :

- Oral Glucose Suppression Test : Fasting and resting patients and normal volunteers were given 50 gm glucose orally at 8.00 am. Blood samples for serum glucose and human growth hormone were taken immediately before the oral glucose administration and at 30 minutes intervals thereafter for a period of 3 hours.

- Intravenous Insulin Stimulation Test : Fasting and resting patients and normal volunteers were given crystalline insulin, 0.1 units/kg body weight. Blood samples were drawn at 30 minutes intervals for a period of two hours.

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In both tests an indwelling intravenous cannula (intracath.) was inserted into the antecubital vein of the fasting, resting subject at 7.30 am. The intracath was kept open by a slow infusion of normal saline to obtain blood samples during the test period. All samples obtained through the indwelling intracath were centrifuged at 4 degrees centigrade within one hour of collection. Serum glucose was immediately estimated while sera for human growth hormone assay were stored at -20°C until assayed.

Radioimmunoassay of the human growth hormone serum levels was performed by the double antibody technique (14). ^{125}I- labelled human growth hormone, antisera and human growth hormone standards were obtained from the Institute of Bio-Endocrinology, Montreal, Canada.

RESULTS

1) Resting values :

Table (1) shows the fasting human growth hormone levels at rest, at 8.00 am., in hepatosplenic schistosomiasis with and without infantilism and their normal control from the same age group.

Table (1) : Resting values of serum human growth hormone in schisto. patients with and without infantilism and normal controls.

Diagnosis	Serum human growth hormone levels Time : 8.00 Am.
Hepatosplenic schisto. + infantilism	3.966±1.35 (S.D.) Micro IU/ml.
Hepatosplenic schisto. without infantilism	2.818±0.748 Micro IU/ml.
Normal controls	4.3 ± 4 " "
Range of normal resting values	0.00 to 10.0 Micro IU/ml.

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2. Serum human growth hormone response to oral glucose :

Tables (2,3 & 4) and Fig. (1) show an initial paradoxic rise in the mean human growth hormone levels in schistosomiasis patients with infantilism. This was followed by a gradual decrease in human growth hormone levels. The initial rise was replaced by a sluggish fluctuation in human growth hormone levels in schistosomiasis patients without infantilism ,Tables(5 & 6) and Fig. (1). The normal control group showed a definite reduction in human growth hormone serum levels, Table (2) and Fig. (1).

A late rise in mean human growth hormone levels was noticed in the three groups. However in cases with schistosomiasis and infantilism this rise was not only late but also much smaller when compared with that of the other two groups.

Table (2) : Serum human growth hormone response to oral glucose in schistosomiasis patients with and without infantilism and normal controls.

Diagnosis	Mean resting value (mIU/ml) (Min. 0)	Percent Change					
		Min. 30	Min. 60	Min. 90	Min. 120	Min. 150	Min. 180
Hepatosplenic schisto. + infantilism	4.249	+ 4.0	+13.7	-24.9	-21.7	-31.4	+14.8
Hepatosplenic schisto. without infantilism	2.957	-14.2	+ 2.5	-26.0	-21.2	+62.1	+203.7
Normal controls	6.000	-41.7	-66.7	-80.0	-63.3	-33.3	+66.7

Tables (7 & 8) show the effect of glucose loading in patients with hepatosplenic schistosomiasis with infantilism, a mild degree of glucose intolerance with observed as serum glucose levels did not return to their previous fasting levels after 120 min. following glucose administration (+19%). This glucose intolerance was less marked in patients with hepatosplenic schistosomiasis without infantilism (+3%), Tables (9 & 10).

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3. Serum human growth hormone levels during intravenous insulin tolerance test :

In response to intravenous insulin administration, a delayed rise of serum human growth hormone reaching 65% at min 60 and 227% at min 90 was observed in patients with hepatosplenic schistosomiasis and infantilism, Tables (11 & 12) and Fig. (2). In those patients without infantilism the rise started to occur at minute 3o reaching 71% and the peak response occurred at min 60 reaching 581%, Tables (13 & 14) and Fig. (2). In normal controls the peak rise in mean human growth hormone levels also occurred at min. 60 reaching 814%, Tables (19 & 20) & Fig. (2).

The serum glucose response to intravenous insulin was delayed and blunted in patients with hepatosplenic schistosomiasis with infantilism, reaching a nadir at min. 90 of only -35% of the initial value, Tables (15 & 16). In both normal controls and patients with hepatosplenic schistosomiasis without infantilism the nadir of hypoglycemia occurred at min. 30 reaching below -50% of the initial mean value, Tables (17 & 18).

DISCUSSION :

Paradoxical growth hormone secretion in response to oral glucose was reported in hepatosplenic schistosomiasis (6 , 15). However the present findings show that this paradoxical response occurred in patients with hepatosplenic schistosomiasis with infantilism.

The mechanism of this phenomenon is not clear, but it is possible that oestrogens, known to be poorly inactivated in hepatic cirrhosis, induce the elevated human growth hormone levels. The findings (16) may be of relevance to this problem. They found that some degree of carbohydrate intolerance together with failure of growth hormone response were observed in normal controls subjected to stress. It is therefore possible that inadequate response to oral glucose may be due to the inability of the pituitary to respond subsequent to some pre-investigational stress viz. the schistosomal infection.

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The association of various disturbances of carbohydrate metabolism with chronic liver disease has been frequently reported (17,18). Abnormalities in the patterns and quantitative responses of these hormones to glucose loading was shown in post-necrotic cirrhosis, hepatitis and alcoholic liver cirrhosis (19,20,21). In hepatic schistosomiasis, where lesions tend to affect the portal tract and spares the liver parenchyma, a degree of glucose intolerance was reported to occur even before the development of ascites and was not related to the severity of liver damage as revealed by liver function tests (15,22). Abnormal growth hormone secretion during the absorptive phase of glucose load may at least in part account for the impaired glucose tolerance (15).

Several explanations for hepatogenous glucose intolerance in chronic liver disease are available. Portal systemic shunts have been described to contribute to disturbances in carbohydrate metabolism (17, 21) and the development of insulin resistance (23). Such insulin resistance might explain the apparent lack of adequate human growth hormone response to intravenous insulin in patients with hepatosplenic schistosomiasis and infantilism.

FIGURE 1. SERUM HUMAN GROWTH HORMONE AND GLUCOSE LEVELS DURING ORAL GLUCOSE TOLERANCE TEST IN SCHISTO. PATIENTS WITH AND WITHOUT INFANTILISM.

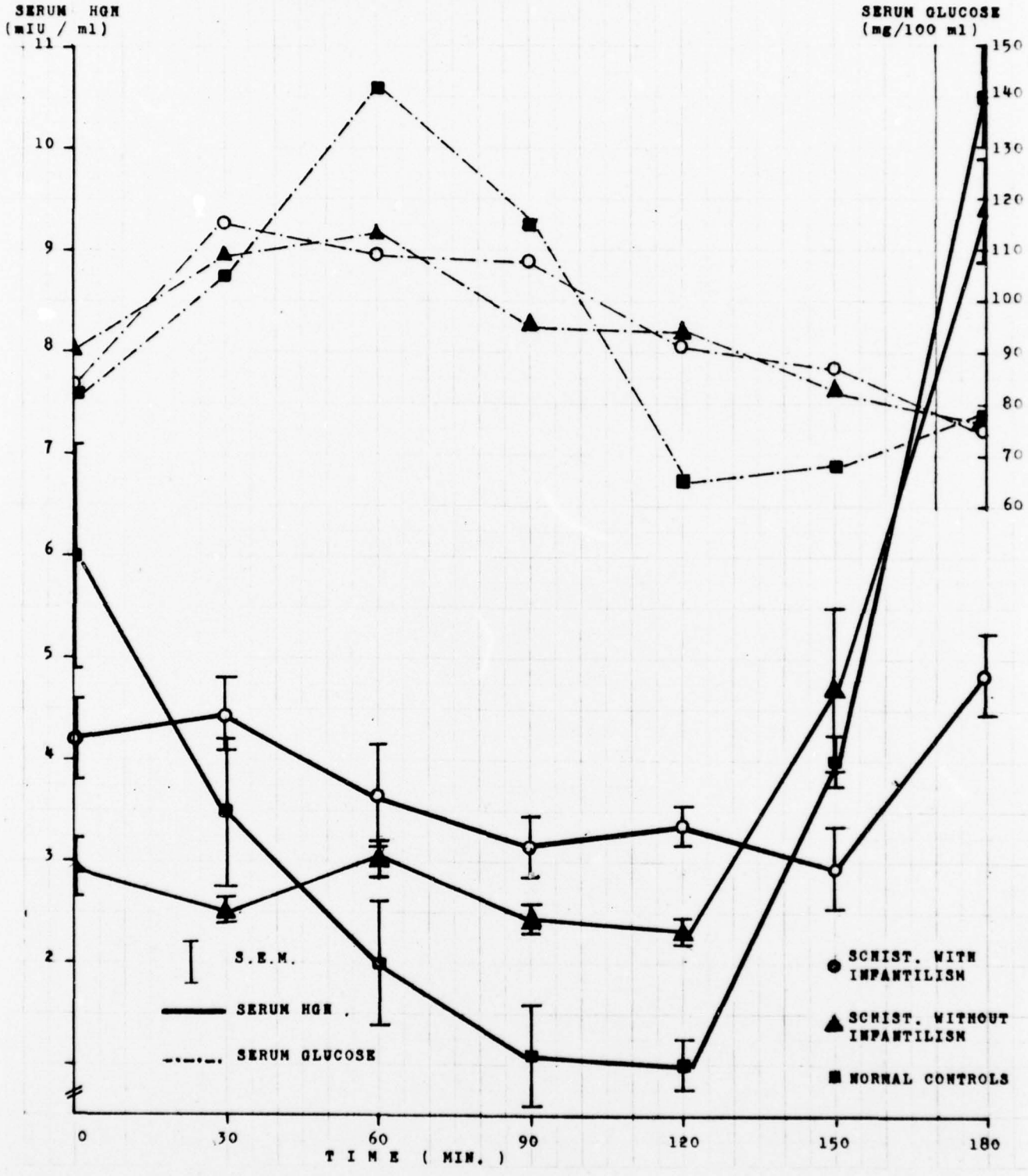

FIGURE 2. SERUM HUMAN GROWTH HORMONE AND GLUCOSE LEVELS DURING INSULIN TOLERANCE TEST IN SCHISTO. PATIENTS WITH AND WITHOUT INFANTILISM.

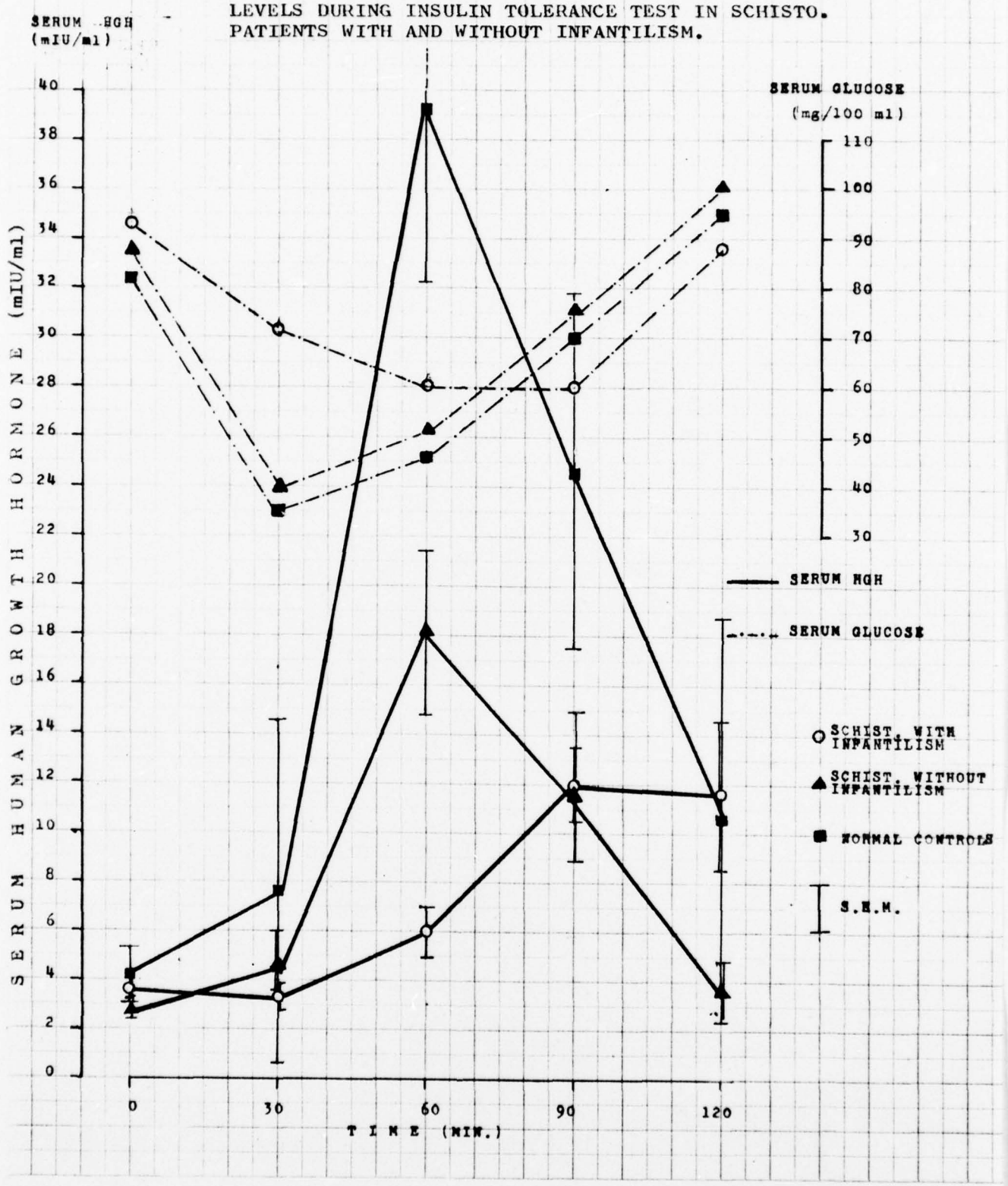

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Table (3) : Serum human growth hormone levels during oral glucose tolerance in hepatosplenic schistosomiasis with infantilism.

Patient	Serum human growth hormone levels (mIU/ml)						
	Min. 0	Min. 30	Min. 60	Min. 90	Min. 120	Min. 150	Min. 180
1	2.027	1.047	1.084	1.337	3.129	0.727	3.733
2	3.636	2.433	2.350	2.447	2.677	1.767	4.300
3	4.672	4.449	4.977	3.504	3.200	3.150	4.000
4	4.010	5.773	5.410	4.188	4.050	4.200	5.500
5	4.400	4.886	4.244	3.434	3.734	3.722	5.948
6	5.400	6.685	5.297	4.401	4.438	4.795	7.374
7	4.150	4.139	2.786	3.197	2.598	2.850	5.000
8	5.700	5.952	3.211	3.051	2.783	2.100	3.150
Mean	4.249	4.421	3.669	3.192	3.326	2.914	4.876
S.D.	1.350	1.149	1.564	1.970	0.679	1.345	1.372
S.E.	0.401	0.406	0.553	0.343	0.240	0.476	0.485

Table (4) : Percent change in serum human growth hormone levels during oral glucose tolerance in hepatosplenic schistosomiasis with infantilism.

Patient	Initial level (mIU/ml)	Percent change					
		%	%	%	%	%	%
1	2.027	-48.347	-46.522	-34.041	+54.366	-64.134	+84.164
2	3.636	-33.086	-35.368	-32.701	-26.375	-51.403	+18.262
3	4.672	- 4.773	+ 6.421	-25.000	-31.507	-32.577	-14.384
4	4.010	+43.965	+34.913	+ 3.940	+ 0.998	+ 4.738	+37.157
5	4.400	+11.046	- 3.545	-21.955	-15.136	-15.409	+35.181
6	5.400	+23.796	- 1.907	-18.500	-17.815	-11.204	+36.560
7	4.150	- 0.265	-32.867	-22.964	-37.398	-31.325	+20.482
8	5.700	+ 4.421	-43.667	-46.474	-51.175	-63.158	-44.737
Mean	4.249	+ 4.048	-13.650	-24.876	-21.723	-31.419	+14.756

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Table (5) : Serum human growth hormone levels during oral glucose tolerance in schistosomal hepatic fibrosis without infantilism.

Patient	Serum human growth hormone levels (m IU/ml)						
	Min. 0	Min. 30	Min. 60	Min. 90	Min. 120	Min. 150	Min. 180
1	2.391	2.359	3.214	2.597	2.586	5.177	13.746
2	2.448	2.359	3.394	2.684	2.052	4.956	16.469
3	2.535	2.278	3.279	2.554	2.600	7.720	-
4	2.553	2.736	3.708	2.487	2.680	6.374	-
5	4.094	2.722	2.479	2.402	1.879	1.989	2.826
6	3.719	2.760	2.208	2.402	2.191	2.546	2.884
Mean	2.957	2.536	3.030	2.485	2.331	4.794	8.981
S.D.	0.748	0.225	0.573	0.174	0.335	2.198	7.160
S.E.	0.305	0.092	0.234	0.071	0.136	0.897	3.580

Table (6) : Percent change in serum human growth hormone levels during oral glucose tolerance in schistosomal hepatic fibrosis without infantilism.

Patient	Initial level (mIU/ml)	Percent change					
		%	%	%	%	%	%
1	2.391	- 1.338	+30.238	+ 8.616	+ 8.156	+116.520	+474.906
2	2.448	- 3.636	+38.644	+ 9.641	-16.176	+102.451	+572.753
3	2.535	-10.138	+29.349	+ 0.750	+ 2.564	+204.536	-
4	2.553	+ 7.168	+45.241	- 2.585	+ 4.975	+149.667	-
5	4.094	-33.512	-39.448	-46.580	-54.114	-51.417	- 30.972
6	3.719	-25.787	-40.629	-35.413	-41.086	-31.541	- 22.452
Mean	2.957	-14.237	+ 2.469	-25.962	-21.170	+62.123	+205.720

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Table (7) : Serum glucose levels during oral glucose tolerance test in hepatosplenic schistosomiasis with infantilism.

Patient	Serum human growth hormone levels (mg/dl)						
	Min. 0	Min. 30	Min. 60	Min. 90	Min. 120	Min. 150	Min. 180
1	92	115	116	112	98	90	82
2	78	100	112	132	123	105	74
3	80	145	83	78	78	80	73
4	90	131	95	92	80	69	63
5	80	97	144	124	97	82	71
6	95	130	129	109	87	97	79
7	81	102	101	90	78	85	80
8	78	105	95	129	93	80	84
Mean	84.250	115.375	109.375	108.250	91.75	86.000	75.750
S.D.	6.902	17.246	10.049	19.890	15.04	11.187	6.881
S.E.	2.440	6.097	7.088	7.032	5.318	3.955	2.433

Table (8) : Percent change in serum glucose levels during oral glucose tolerance in hepatosplenomegaly with infantilism.

Patient	Initial level (mg/dl)	Percentage change					
		%	%	%	%	%	%
1	92	+25.00	+26.09	+21.74	+ 6.00	- 2.17	-10.04
2	78	+28.20	+43.59	+69.23	+57.69	+34.62	- 5.13
3	80	+78.75	+ 3.75	- 2.50	- 2.50	00.00	- 8.75
4	90	+45.56	+ 5.56	+ 2.22	-11.11	-23.33	-30.00
5	80	+ 7.78	+60.00	+37.78	+ 7.78	- 8.89	-21.11
6	95	+36.84	+35.79	+14.74	- 8.42	+ 2.12	-16.84
7	81	+25.93	+14.69	+11.11	- 3.71	+ 4.93	- 1.24
8	78	+34.62	+21.79	+65.38	+19.23	+ 2.56	+ 7.69
Mean	84.250	+36.94	+29.82	+28.49	+ 8.90	+ 2.07	-10.10

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Table (9) : Blood sugar values during oral glucose tolerance in schistosomal hepatic fibrosis without infantilism.

Patient	Blood sugar values (mg/100 ml)						
	Min. 0	Min. 30	Min. 60	Min. 90	Min. 120	Min. 150	Min. 180
1	79	102	99	96	95	90	70
2	91	123	118	107	104	95	84
3	107	118	126	85	88	67	74
4	87	93	119	97	84	76	80
5	100	118	121	98	95	90	87
6	83	104	101	97	99	94	80
Mean	91.20	109.7	114.00	96.700	94.20	83.70	79.20
S.D.	10.590	11.708	11.207	7.005	7.250	10.150	6.174
S.E.	4.324	4.780	4.575	2.860	2.960	4.185	2.262

Table (10) : Percent change in blood sugar during oral glucose tolerance in schistosomal hepatic fibrosis without infantilism.

Patient	Initial level (mg/100 ml)	Percentage change					
		%	%	%	%	%	%
1	79	29.114	25.316	21.509	20.253	13.924	-11.392
2	91	35.165	29.670	17.580	14.290	- 6.590	- 7.690
3	107	10.280	17.760	-20.560	-17.760	-37.380	-30.840
4	87	6.890	36.780	11.490	- 3.450	-12.640	- 8.050
5	100	18.000	21.000	- 2.000	- 5.000	-10.000	-13.000
6	83	25.300	21.690	16.870	19.280	13.260	- 3.600
Mean	91.20	20.290	25.000	6.000	3.290	- 8.200	-13.160

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Table (11) : Serum human growth hormone levels during intravenous insulin tolerance test in patients with schistosomal hepatic fibrosis and infantilism.

Patient	Serum human growth hormone levels (mIU/ml)				
	Min. 0	Min. 30	Min. 60	Min. 90	Min. 120
1	3.103	4.698	8.709	8.269	7.652
2	2.419	1.103	3.170	15.308	21.081
3	3.390	3.502	4.660	12.210	17.000
4	4.489	3.218	5.138	8.850	19.000
5	5.008	4.946	8.717	8.130	6.374
Mean	3.6818	3.493	6.0788	12.044	11.702
S.D.	1.052	1.520	2.512	3.565	7.316
S.E.	0.470	0.684	1.123	1.595	3.272

Table (12) : Percent change in serum human growth hormone levels during intravenous insulin tolerance test in patients with schistosomal hepatic fibrosis and infantilism.

Patient	Initial level (mIU/ml)	Percent change			
		%	%	%	%
1	3.103	+51.402	+180.664	+166.484	+146.600
2	2.419	-54.403	+ 31.046	+532.823	+771.476
3	3.390	+ 3.304	+ 37.460	+260.177	+401.475
4	4.489	-28.314	+14.457	+252.020	+323.257
5	5.008	- 1.238	+ 74.060	+ 62.340	+ 27.280
Mean	3.6818	- 5.127	+ 65.100	+ 227.123	+217.834

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Table (13) : Serum human growth hormone levels during intravenous insulin tolerance test in patients with schistosomal hepatic fibrosis without infantilism.

Patient	Serum human growth hormone levels (mIU/ml)				
	Min. 0	Min. 30	Min. 60	Min. 90	Min. 120
1	2.973	2.941	17.752	8.039	4.257
2	1.750	2.161	27.634	20.421	3.520
3	3.143	8.770	15.530	10.651	6.179
4	2.845	4.500	12.022	8.430	7.782
Mean	2.678	4.593	18.235	11.885	3.623
S.D.	0.630	2.950	6.696	5.806	2.843
S.E.	0.325	1.474	3.348	2.903	1.321

Table (14) : Percent change in serum human growth hormone levels during intravenous insulin tolerance test in patients with schistosomal hepatic fibrosis without infantilism.

Patient	Initial level (mIU/ml)	Percent change			
		%	%	%	%
1	2.973	1.076	497.107	170.400	43.189
2	1.750	23.485	1479.086	1066.914	101.143
3	3.143	179.033	394.114	238.880	96.595
4	2.845	58.172	322.566	196.309	173.533
Mean	2.678	71.509	580.919	343.801	35.288

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Table (15) : Blood sugar values during intravenous insulin tolerance test in patients with schistosomal hepatic fibrosis and infantilism.

Patient	Blood sugar value (mg/100 ml)				
	Min. 0	Min. 30	Min. 60	Min. 90	Min. 120
1	98	57	59	54	78
2	103	91	67	66	99
3	95	69	74	83	90
4	82	64	45	40	98
5	89	82	62	60	75
Mean	93.40	72.60	61.40	60.60	88.00
S.D.	8.142	13.759	10.784	15.805	11.43
S.E.	3.641	6.153	4.823	7.068	4.970

Table (16) : Percent change in blood sugar values during intravenous insulin tolerance test in patients with schistosomal hepatic fibrosis and infantilism.

Patient	Initial level (mg/100 ml)	Percentage change			
		%	%	%	%
1	98	-41.835	-39.796	-44.898	-20.408
2	103	-11.650	-34.950	-35.950	- 3.880
3	95	-27.368	-22.110	-12.630	- 5.260
4	82	-21.950	-45.120	-51.210	-19.512
5	89	- 7.865	-30.337	-32.584	-15.730
Mean	93.40	-22.270	-34.260	-35.120	- 5.780

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Table (17) : Blood sugar levels during insulin tolerance test in patients with schistosomal hepatic fibrosis without infantilism.

Patient	Blood sugar (mg/100 ml)				
	Min. 0	Min. 30	Min. 60	Min. 90	Min. 120
1	92	36	117	70	78
2	85	39	20	63	110
3	88	41	24	64	95
4	87	45	47	107	122
Mean	88	40.250	52.00	76	101.25
S.D.	2.944	3.775	44.936	20.897	19.033
S.E.	1.472	1.887	22.468	10.448	9.516

Table (18) : Percent change in blood sugar levels during insulin tolerance test in patients with schistosomal hepatic fibrosis without infantilism.

Patient	Initial level (mg/100 ml)	Percentage change			
		%	%	%	%
1	92	-60.869	+27.174	-23.91	-15.210
2	85	-54.120	-76.470	-25.88	+29.411
3	88	-53.400	-72.730	-27.27	+ 7.950
4	87	-48.280	-45.980	+22.99	+40.230
Mean	88	-54.260	-40.900	-13.64	+15.060

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Table (19) : Serum human growth hormone levels during insulin tolerance test in normal controls.

Patient	Serum human growth hormone levels(mIU/ml)				
	Min. 0	Min. 30	Min. 60	Min. 90	Min. 120
1	3.0	2.0	42.0	30.0	24.0
2	6.5	9.0	44.0	34.0	16.5
3	5.0	57.0	15.0	6.0	50.0
4	2.0	11.5	65.0	52.5	25.0
5	8.5	11.0	21.0	10.0	3.5
6	1.0	7.0	49.0	15.0	9.5
Mean	4.3	7.7	39.3	24.5	10.6
S.D.	2.857	22.318	18.491	17.590	20.128
S.E.	1.167	9.111	7.548	7.181	8.217

Table (20) : Percent change in serum human growth hormone levels during insulin tolerance test in normal controls.

Patient	Initial level (mIU/ml)	Percent change			
		%	%	%	%
1	3.0	-33.33	+1300.0	+ 900	+700.0
2	6.5	+38.5	+ 570.4	+ 423	+153.9
3	5.0	+1040	+200	+ 20	+900.0
4	2.0	+475.0	+ 315.0	+2525	+1150
5	8.5	+ 29.0	+ 147.0	+ 17.7	- 58.8
6	1.0	+600.0	+4800.0	+1400.0	+ 850.0
Mean	4.3	+ 79.1	+ 813.9	+ 469.77	+ 146.51

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PART II : PLASLA A.C.T.H. AND CORTISOL LEVELS DURING INSULIN-INDUCED HYPOGLYCEMIA IN HEPATOSPLENIC SCHISTOSOMIASIS :

The altered hormonal pattern of the human growth hormone (Part I) led to investigate the pituitary adrenal axis in the same patient group. It has been acknowledged by many authors that corticosteroids may inhibit statural growth (24,25). Other reports point out that the metabolic response of corticosteroids treated children to exogenous human growth hormone was much impaired (26).

In hepatosplenic schistosomiasis, the adrenal glands react by a normal oesinophilic response to ACTH stimulation, but not by the expected 17-Ketosteroids increased excretion (27). They concluded that there is a normal pituitary adrenal axis and they suggested the possibility of an arrest of synthesis of steroids by the adrenal glands or the testes and/or an abnormal enzymatic degradation of these steroids by the hepatic cells leading to different metabolites. Other reports suggested that a) the diminished urinary 17-Ketosteroids in schistosomal hepatic fibrosis is due to an elevated blood estrogens level inhibiting leutinizing hormone and possibly ACTH secretion leading to diminished testicular and adrenal androgens production (28) and b) normal plasma cortisol, low normal 17-Ketogenic steroids, low 17 ketosteroids and high urinary oestriol levels in schistosomiasis patients (29).

MATERIALS AND METHODS :

Seven male patients with hepatosplenic schistosomiasis associated with infantilism were compared with two male patients with hepatosplenic schistosomiasis without evidence of retardation of growth or sexual development. Six normal control subjects were also selected. All individuals subjected to this study were of the same group (14 ± 1.5 years).

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Plasma ACTH Measurement :

Extraction of plasma ACTH was performed by modified silicic acid adsorption method (30) with modifications, ^{125}I-ACTH was added to 1 ml of plasma sample to be analyzed and then mixed completely with approximately 12 mg of silicic acid with vortex mixer. After washing the silicic acid twice with 1 ml of 0.5% human serum albumin, ACTH was eluted with 0.4 ml of a 1 : 10 mixture of acetone : 0.01 N aquous hydrochloric acid. The supernate was transfered to a polypropylene incubation vial in which 0.1 ml of 0.2 M borate buffer pH 8.4 and 0.05 ml of 0.5 N sodium hydroxide solution were added in advance. To this extract 0.05 ml of antiserum was added.

The final dilution of the antiserum used was 1 : 40,000. The mixture was incubated for 4 days at 4°C. Antibody-bound and free fractions were separated by talc adsorption. In order to construct a standard curve, known amounts, ranging from 0 to 400 pg, of synthetic 1-39 ACTH were added to dexamethasone suppressed plasma, extracted and assayed in the same manner as the samples. Antibody bound and free ratio was then plotted against the amount of ACTH added to plasma.

Plasma Cortisol Measurement :

The plasma cortisol was measured by competitive protein binding method (31).

RESULTS AND DISCUSSION :

Plasma cortisol and ACTH levels during insulin tolerance test in patients with schistosomiasis and infantilism were compared with normal controls. They were also compared with one case of a) pituitary infantilism, b) Addisson's disease, c) Post-pituitary ablation and d) adrenogenital tumour (Fig. 3 & 4).

The mean fasting resting level of plasma ACTH and cortisol in schisto. patients with infantilism was within the normal range and concur with earlier reports (29,2). However, these normal resting levels did not show an adequate rise when insulin was administrated, Table (21). Furthermore, a educed and delayed hypoglycemic

response to intravenous insulin was observed in schistosomal patients with infantilism, Fig. 3,4 & 5 and Tables (23-28). In normal controls the same insulin dose produced marked hypoglycemia at minute 30 (68% drop). It produced an increase in ACTH and cortisol level reaching a 2-fold increase above the fasting level 30 minutes after the glucose nadir (Fig. 3). Earlier reports suggested the possibility of an arrest of synthesis of steroids by the adrenal gland or the testes and/or an abnormal enzymatic degradation of these steroids by hepatic cells leading to different metabolites (27).

If these earlier suggestions were correct then the feed-back mechanism of the hypothalamic pituitary adrenocortical axis should lead to very high ACTH blood levels. However our findings show that the expected rise in ACTH blood levels in response to insulin induced hypoglycaemia was either absent or inadequate (Fig.3). These findings conform with those of Peterson et al. who were the first to suggest, among other suggestions, a) decreased production of ACTH in acute viral hepatitis and other ferms of liver and biliary disease and b) depressed adrenocorticol functions (32).

STUDIES ON PITUIT. FUNCT. IN HEPATIC AND PULMONARY SCHISTOSOMIASIS

SERUM CORTISOL LEVELS DURING INSULIN TOLERENCE TEST

ASSAYS #7, 8, 14, 15
PROT. #01
CODE: DELTA 02

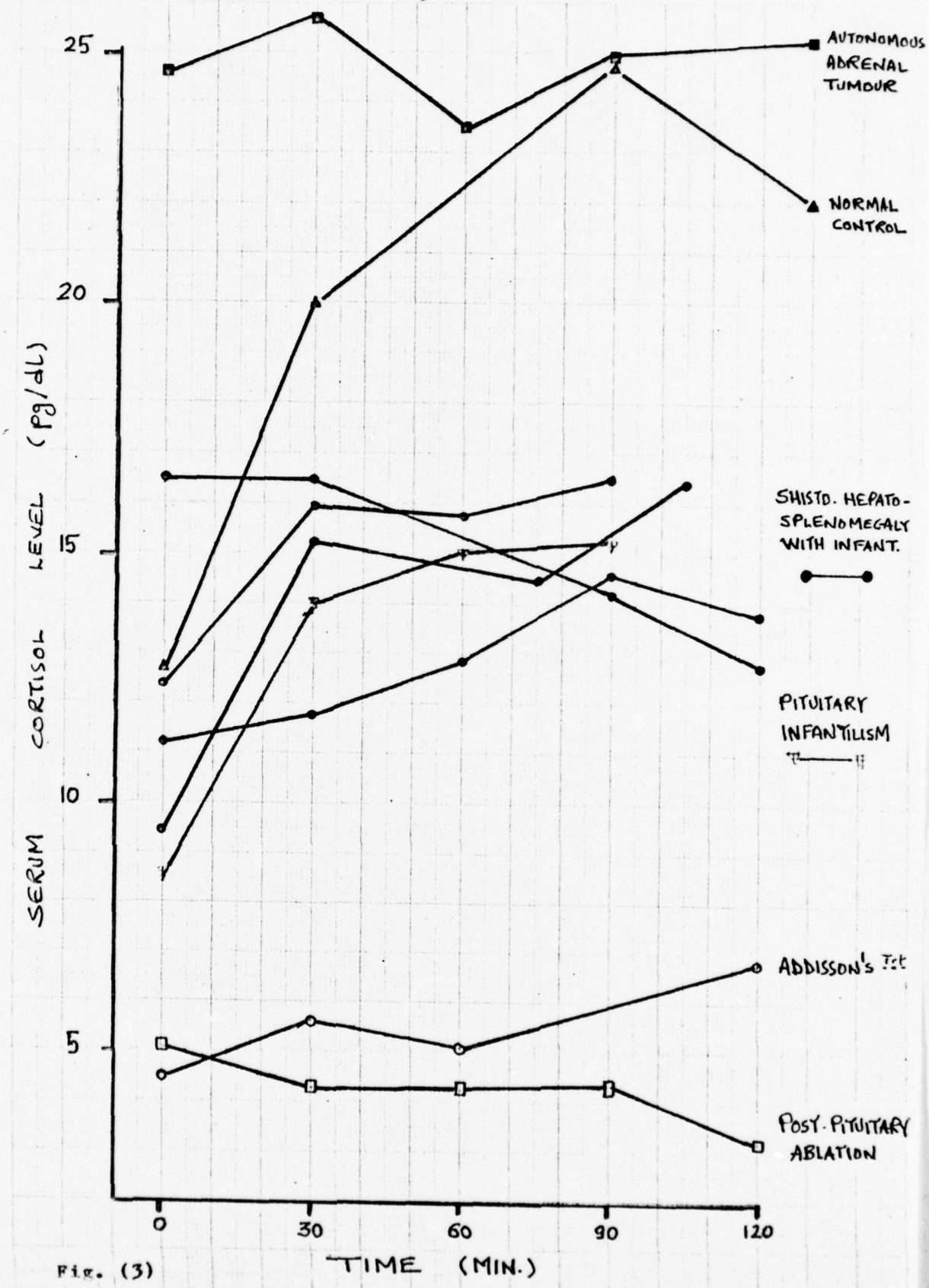

Fig. (3)

PITUIT. FUNCTIONS IN HEPATIC AND PULMONARY SCHIST.

SERUM CORTISOL AND GLUCOSE LEVELS DURING INSULIN TOLERENCE TEST.

RIA # 7,8, 14,15
PROT. # 001
CODE: DELTA 02

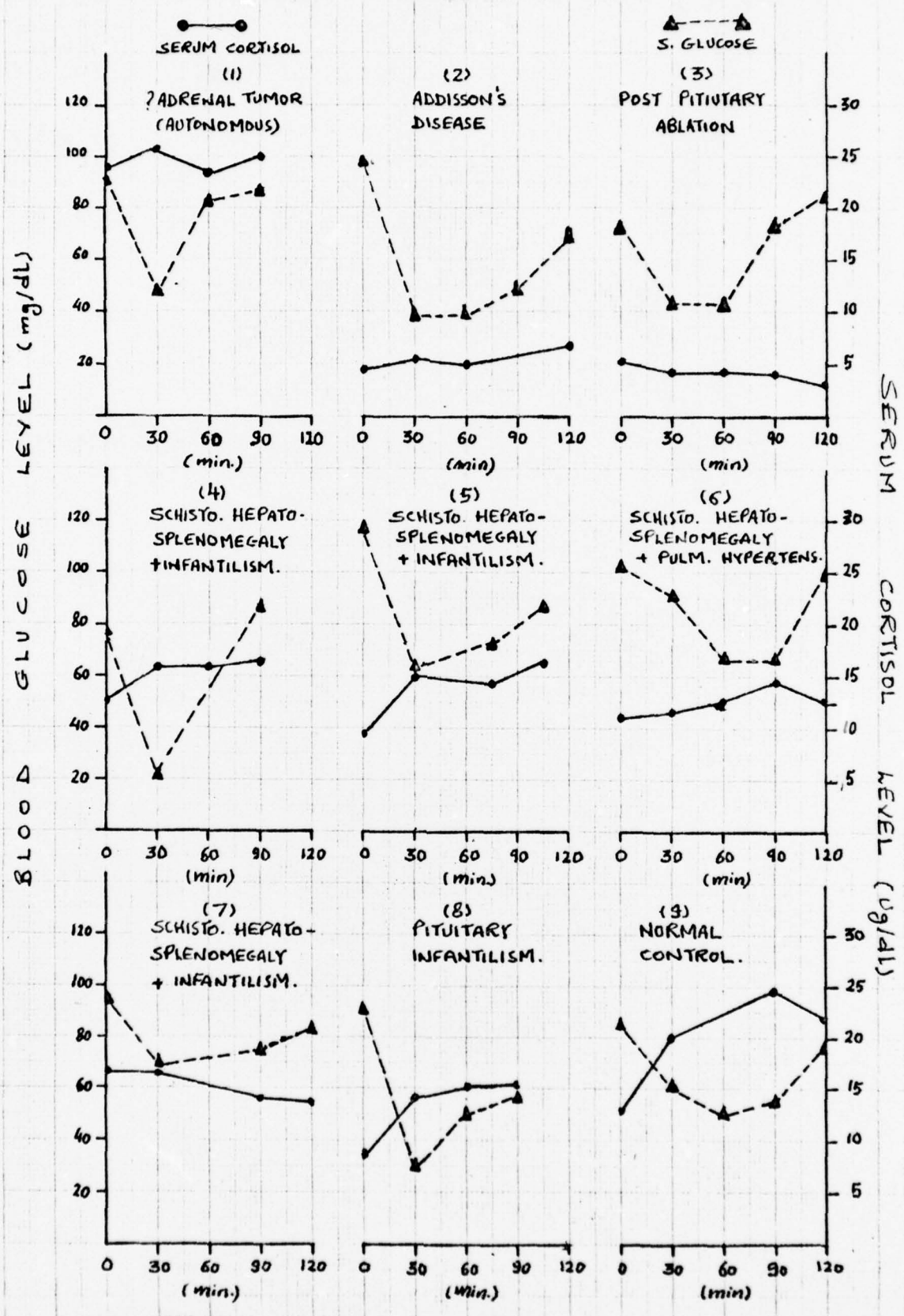

Fig. (4)

ASSAY # 16
PROT # 03
CODE: DELTA 02

PITUIT. FUNCT. IN HEPATIC AND PULMONARY SCHISTOSOMIASIS

IMMUNO REACTIVE ACTH PLASMA LEVELS DURING INSULIN TOLERENCE TEST

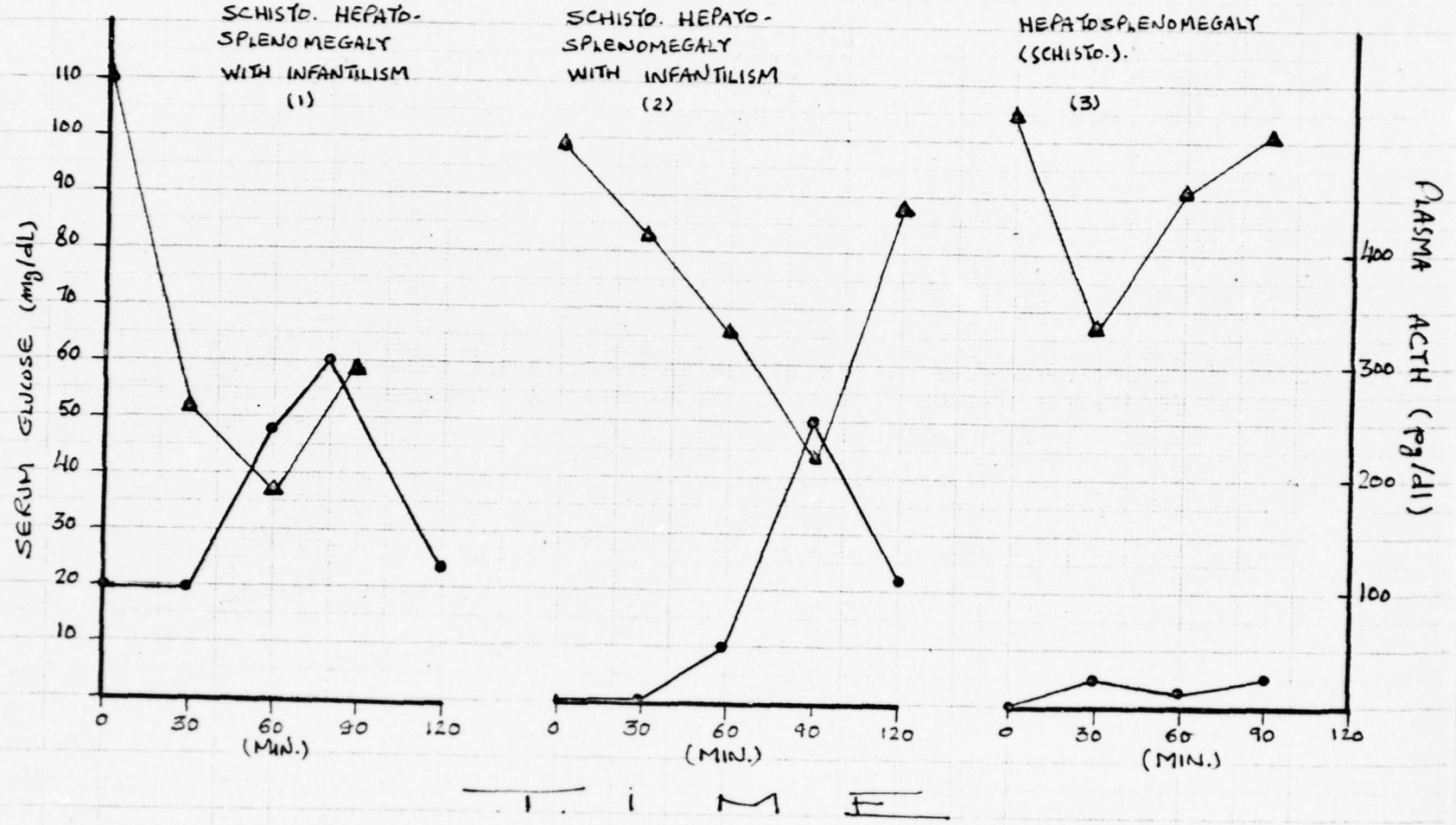

Fig. (5)

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Table (21) : Plasma ACTH levels (pg/ml) during insulin tolerance test in patient with schistosomal hepatic fibrosis and infantilism.

Patient	ACTH plasma (pg/ml)				
	Min. 0	Min. 30	Min. 60	Min. 90	Min. 120
1	60	78.0	67.2	42.0	24.0
2	9.6	34.8	31.2	30.0	10.8
3	0.0	103.2	76.8	24.0	12.0
4	0.0	120.0	54.0	34.32	12.96
5	35.52	66.0	14.4	-	-
6	36.0	60.0	35.04	-	-
7	0.0	11.52	12.0	11.52	11.04
Mean	20.171	67.646	41.52	28.368	14.16
S.D.	23.821	37.422	25.226	11.476	5.566
S.E.	9.004	14.133	9.531	5.133	2.489

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Table (22) : Serum cortisol levels during insulin tolerance test in schistosomal patients with infantilism.

Patient	Plasma Cortisol (mcg/100 ml)			
	Min. 0	Min. 30	Min. 60	Min. 90
1	12.5	16.0	16.0	16.5
2	4.5	15.0	14.5	17.0
3	11.0	11.4	12.9	14.6
4	17	17.0	-	14.0
Mean	11.2	14.8	14.4	15.4
S.D.	5.172	2.441	1.552	1.457
S.E.	2.586	1.220	0.896	0.729

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Table (23) : Blood sugar levels during insulin tolerance test in patients with hepatosplenic schistosomiasis and infantilism.

Patient	Blood sugar values (mg/100 ml)				
	Min. 0	Min. 30	Min. 60	Min. 90	Min. 120
1	97	38	85	143	120
2	85	49	106	99	62
3	74	55	66		
4	105	67	91	101	
Mean	90.25	52.25	113.5	114.33	91.00
S.D.	13.598	12.093	34.789	24.846	41.01
S.E.	6.799	6.046	17.395	14.345	28.99

Table (24) : Percent change in blood sugar levels during insulin tolerance test in patients with hepatosplenic schistosomiasis and infantilism.

Patient	Initial level (mg/100 ml)	Percent change			
		%	%	%	%
1	97	-60.8	-12.4	+47.4	+23.7
2	85	-42.4	+24.7	+16.5	-27.1
3	74	-25.7	-10.8	-	-
4	105	-36.2	-13.3	- 3.8	-
Mean	90.25	-42.1	+25.76	+26.68	+ 1.0

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Table (25) : Plasma ACTH levels during insulin tolerance test in patients with hepatosplenic schistosomiasis without infantilism.

Patient	Plasma ACTH levels (pg/100 ml)				
	Min. 0	Min. 30	Min. 60	Min. 90	Min. 120
1	13.57	14.28	20.14	39.85	21.57
2	00.00	6.42	41.07	19.64	43.21
Mean	6.79	10.35	30.61	29.39	32.39
S.D.	9.595	5.557	14.799	14.299	15.301
S.E.	6.785	3.929	10.465	10.111	10.819

Table (26) : Percent change in plasma ACTH levels during insulin tolerance test in patients with hepatosplenic schistosomiasis without infantilism.

Patient	Initial level (pg/100 ml)	Percent change			
		%	%	%	%
1	13.57	105.2	148.4	293.7	159
2	0.00	-	-	-	-
Mean	6.79	52.4	350.81	332.8	377.0

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Table (27) : Blood sugar levels during insulin tolerance test in patients with schistosomal hepatic fibrosis without infantilism.

Patient	Blood sugar values (mg/100 ml)				
	Min. 0	Min. 30	Min. 60	Min. 90	Min. 120
1	112	52	37	59	44
2	99	82	66	48	86
Mean	105.5	67	51.5	53.5	65
S.D.	9.192	21.21	20.5	7.78	29.89
S.E.	6.499	15.00	14.499	5.499	20.99

Table (28) : Percent change in blood sugar levels during insulin tolerance test in patients with schistosomal hepatic fibrosis without infantilism.

Patient	Initial level (mg/100 ml)	Percent change			
		%	%	%	%
1	112	-53.6	-66.0	-47.3	-60.7
2	99	-17.3	-32.3	-51.5	-13.1
Mean	105.5	-35.4	-50.2	-49.4	-36.9

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CONCLUSION :

The data obtained from the present study reveal an altered hormonal balance in schistosomiasis viz : human growth hormone, corticotrophin and cortisol and glucose blood levels in response to glucose loading and insulin tolerance test. This deviation from the normal is more marked when schistosomiasis is associated with infantilism.

The present findings support the observation that infantilism or stunted growth affects schistosomiasis patients when the infection occurs early in life, that is before adolescence. However, the altered hormonal response of these hormones is still present, but to a milder degree in schistosomiasis patients who were infected after adolescence. This altered hormonal balance may be one of the factors why the mean hight of individuals from countries with endemic schistosomiasis is less than that of individuals from countries free from schistosomiasis whose hight has even increased during the last few decades.

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TECHNICAL REPORT NUMBER III

MULTIPLE MEASURES OF CARDIAC OUTPUT BY THERMODILUTION DURING MITRAL COMMISSUROTOMY, LEFT VENTRICULAR AND CORONARY ANGIOGRAPHY ✱

By

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MULTIPLE MEASURES OF CARDIAC OUTPUT BY THERMODILUTION DURING MITRAL COMMISSUROTOMY, LEFT VENTRICULAR AND CORONARY ANGIOGRAPHY ★

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The objective of this study was to obtain multiple measures of cardiac output, heart rate and stroke volume by KHALIL thermodilution catheter during mitral commissurotomy, left ventricular and coronary angiography.

While studies of coronary artery angiography frequently showed a transient rise of 1 L/min for few minutes after "Hyopaque" injection into left or right coronary artery, (Table 1), left ventricular angiography studies in patients with rheumatic heart disease with either mitral stenosis or double mitral affection did not show any significant change except in one case where this rise was associated with tachycardia of 115/min. (Table 2).

During mitral commissurotomy, (Table 3) measurement of cardiac output and stroke volume showed an immediate transient rise in the cardiac output from 3.82 L/min with stroke volume of 40 ml/min to 6.71 L/min and a stroke volume of 76 ml/min. This was followed by a steady value of 5.04 - 5.07 L/min until both lungs were inflated when the cardiac went up further to 6.36 L/min with a stroke volume of 77.5 ml/min. As the patient developed pyrexia of 38.2°C during the following two days while the catheter was still in situ, values of cardiac output increased to 8.00 L/min and the stroke volume reached 80 ml/min showing a considerable rise when compared with the pre-operative values of cardiac output of 3.8 L/min and a stroke volume of 40 ml/min.

These thermodilution studies show the practical value of obtaining multiple measures of cardiac output, heart rate and stroke volume during mitral commissurotomy as well as during coronary angiography in Ischaemic heart disease and left ventricular angiography in Rheumatic heart disease.

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TABLE (1) : REPEATED DETERMINATION OF CARDIAC OUTPUT BY THERMODILUTION

1st Coronary Study, Male 45 years

Obs. No.	Volts	Rate Watts	Cal/ Min.	Temp. rise °C	Mean Heart Rate	Cardiac Output (Liters) Minute vol.	Cardiac Output Stroke Vol. (ml.)	Remarks
1	38	29	410	.106	80	4.26	53.2	Before injection
2	38	29	410	.107	82	4.22	51.4	Before injection
3	38	29	410	.079	82	5.72	69.7	2 min. after Rt. coronary injec.
4	38	29	410	.071	84	6.37	75.8	40 sec. after 2nd injection into Rt. coronary.
5	38	29	410	.079	86	5.72	66.5	2 min. later
								--- 15 minutes internal
6	38	29	410	.083	82	5.45	66.4	Before injection
7	38	29	410	.081	82	5.39	64.1	1 min.after Lt.coronary injection
8	38	29	410	.081	82	5.58	68.0	2 min.after " " "
9	38	29	410	.0795	85	5.69	66.9	3 min. " " " "
2nd Coronary Study, Male 50 years								
1	38	29	410	.0810	115	5.58	46.5	Supine
2	38	29	410	.070	118	6.46	56.1	Injection
3	38	29	410	.0670	118	6.75	57.2	Supine
4	38	29	410	.0866	118	5.22	43.5	Supine
5	38	29	410	.0796	118	5.68	48.1	Supine
6	38	29	410	.0742	115	6.09	52.9	Supine
7	38	29	410	.0800	120	5.65	47.0	Injection
8	38	29	410	.0730	116	6.19	53.3	1 min. after injection
9	38	29	410	.0615	118	7.35	62.2	2 min. after injection
10	38	29	410	.0620	118	7.29	61.7	3 min. after injection
3rd Coronary Study, Female 28 years								
1	46	42.3	607	.1712	88	5.620	63.9	
2	46	42.3	607	.1272	91	5.170	56.8	Injection
3	42.5	36.1	518	.237	135	2.371	Irregular	
4	41	33.6	482	.1536	95	3.405	35.8	
5	41	33.6	482	.1507	96	3.470	36.1	
6	39	30.4	436	.0920	79	5.150	65.2	

TABLE (2) : REPEATED DETERMINATION OF CARDIAC OUTPUT BY THERMODILUTION

Mitral Stenosis, Female, 32 years

Obs. No.	Volts	Rate Watts	Cal/ Min.	Temp. rise °C	Mean Heart Rate	Cardiac Output (Liters) Minute vol.	Cardiac Output (Liters) Stroke vol. (ml.)	Remarks
1	36.2	26.2	375	.106	90	3.85	42.7	
2	35.38	25.0	358	.110	92	3.54	38.4	
3	36.2	26.2	375	.118	85	3.46	40.7	
4	35.38	25.0	358	.099	90	3.94	43.7	
5	36.2	26.2	375	.107	88	3.82	43.4	
6	36.2	26.2	375	.116	88	3.52	40.0	
Mitral stenosis, Female, 26 years								
1	38	29	410	.142	80	3.18	39.7	Supine
2	38	29	410	.078	110	5.80	52.7	After injection into left ventricle to detect Ml.
Mitral Stenosis with Mild Incompetance, Male, 35 years								
1	37.0	27.3	65	0.106	64	4.05	63.2	Supine
2	37.0	27.3	65	0.105	62	4.05	65.3	Supine
3	36.2	26.2	65	0.092	68	4.44	65.3	During mild exercise
4	36.2	26.2	65	0.098	65	4.17	64.1	Supine

TABLE (3) : REPEATED DETERMINATION OF CARDIAC OUTPUT BY THERMODILUTION BEFORE, DURING AND AFTER MITRAL VALVULOTOMY.

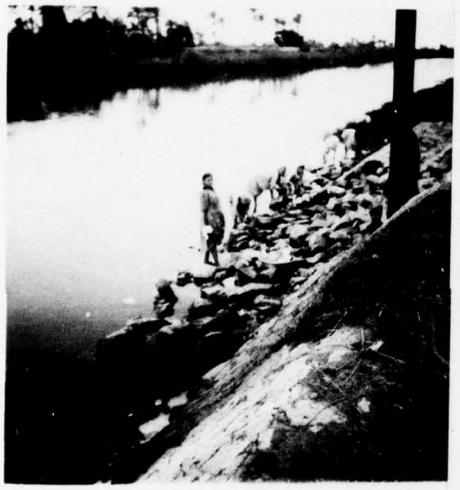
Female, 32 years

	PROGRAM	MEAN HEART RATE	MINUTE VOLUME (Liters)	STROKE VOLUME (Ml.)
1.	Catheterization Lab.	100	3.80	38.0
2.	Catheterization Lab.	100	4.00	40.0
3.	Patient on Right Side	80	3.94	49.0
4.	5 Minutes After Chest was opened	84	4.05	48.0
5.	Percicardium Open	84	5.04	60.0
6.	1 Minute Before Valvulotomy	84	3.82	45.0
7.	After Valvulotomy (immediately)	88	6.71	76.0
8.	Before Lungs Expanded	75	5.04	67.0
9.	Pericardium Fixed? Chest Open	80	5.70	71.0
10.	After Lungs Expanded	82	6.36	77.5
11.	Intensive Care Unit	80	5.45	68.0
12.	3rd Day After Valvulotomy (44 Hours after commissurotomy)	100	8.00	80.0
13.	3rd Day After Valvulotomy (44 Hours after commissurotomy)	100	7.77	77.0

PART NUMBER IV

PHOTOGRAPHS FROM FIELD STUDIES AT PROJECT AREA

A COMMON SIGHT IN THE NILE DELTA : VILLAGERS USING THE LOCAL CANAL FOR THEIR ESSENTIAL DOMESTIC FUNCTIONS, AN INDEX OF THE TRANSMISSION CAPABILITIES OF THE WATER CHANNELS

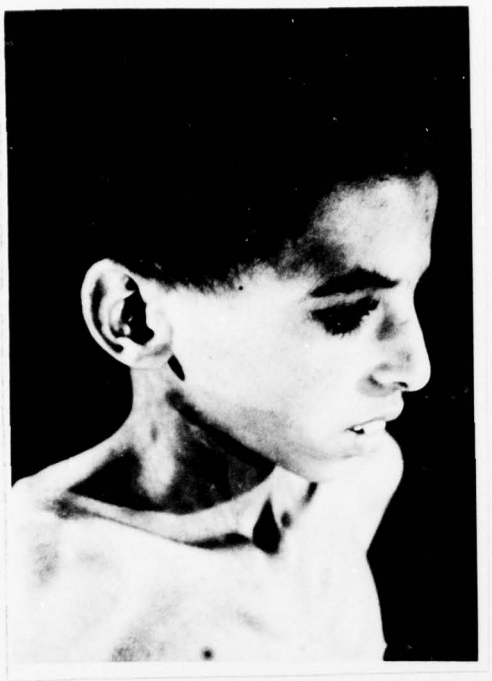


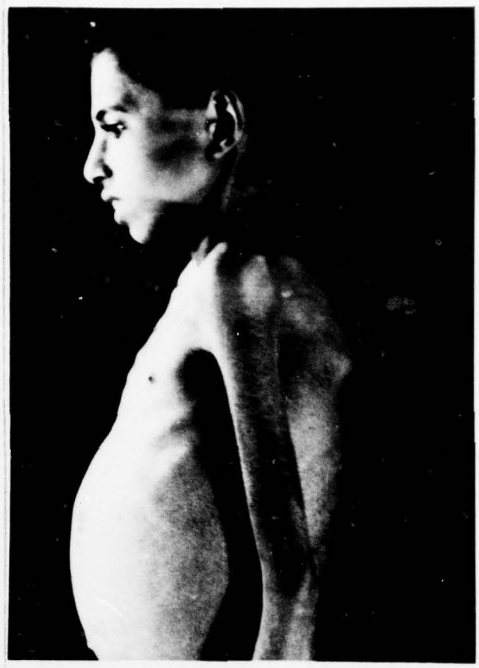
LT: WOMEN WASHING CLOTHES & OTHER DOMESTIC FUNCTION IN THE LOCAL CANAL AT AL-KHADRA VILLAGE.

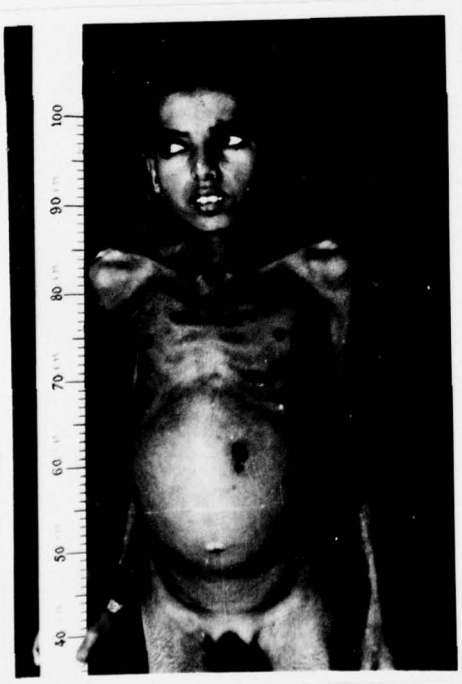
RT: AL-KHADRA VILLAGE HEALTH UNIT NEXT TO A NARROW & SHALLOW CANAL.

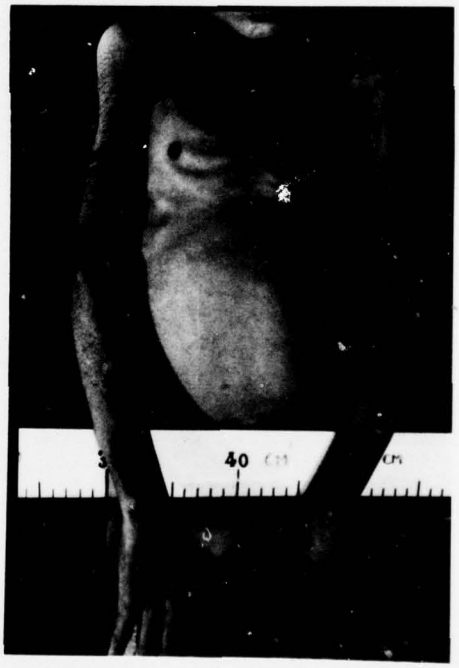
LT: CROWDED CLASSROOM OF AL-KHADRA PRIMARY SCHOOL DURING THEIR MORNING SESSION.

RT: DUE TO LACK OF SPACE: CHILDREN AT AL-KHADRA VILLAGE WAITING FOR THEIR AFTERNOON SESSION

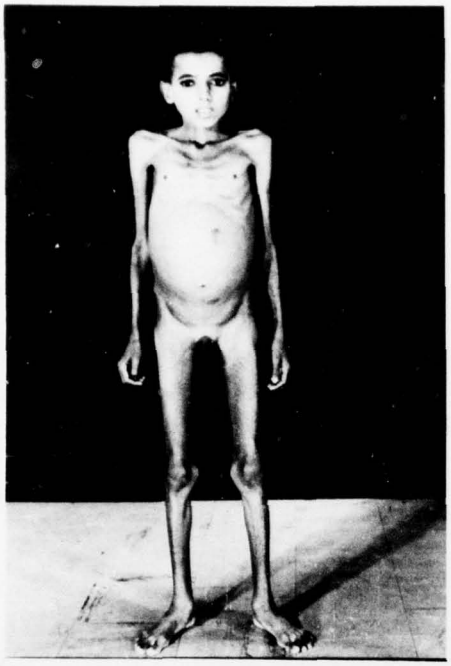


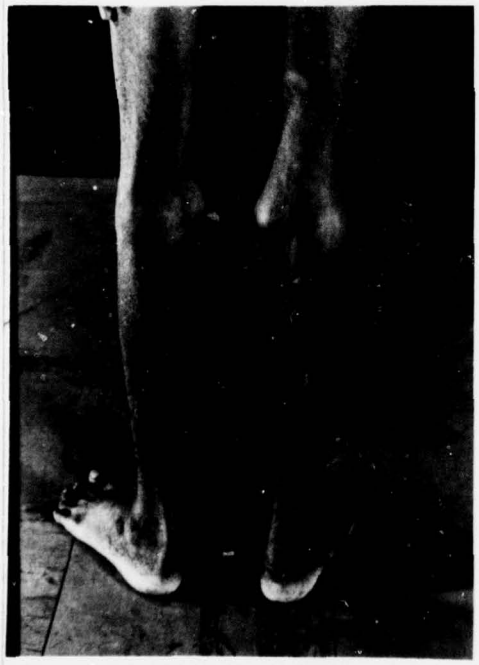


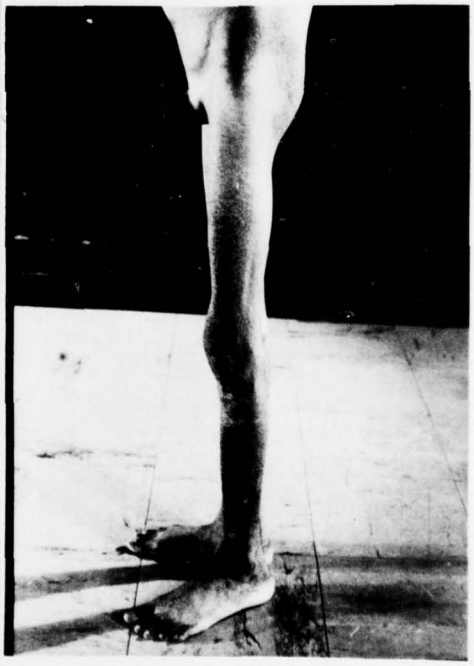




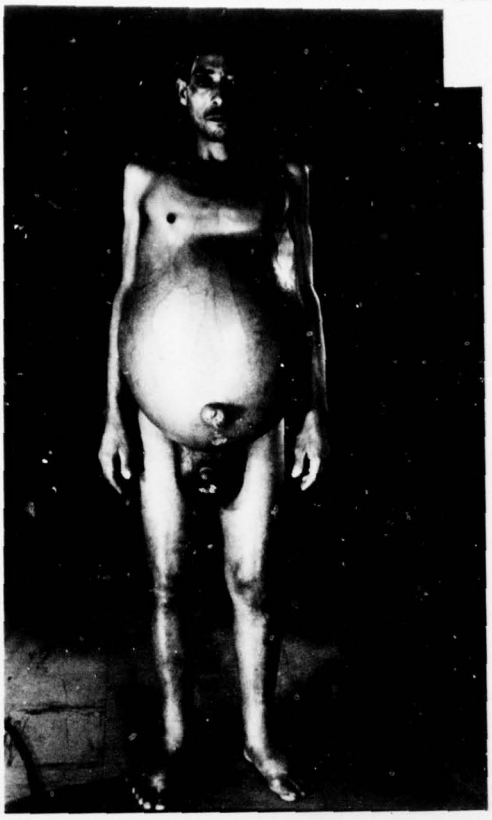
AN ADOLESCENT (AGE: 15 YEARS, HEIGHT: 110 CM.) FROM PROJECT AREA WITH A) EARLY AND REPEATED SCHISTO. INFECTIONS, B) RETARDED GROWTH AND DEVELOPMENT, C) UNDESCENDED TESTICLES, D) SCHISTO. HEPATOSPLENOMEGALY AND ASCITES, E) MARKED MALNUTRITION AND F) EXTENSIVE DERMATOLOGICAL SIGNS OF PELLAGRA OVER BOTH PRESSURE AND EXPOSED AREAS.

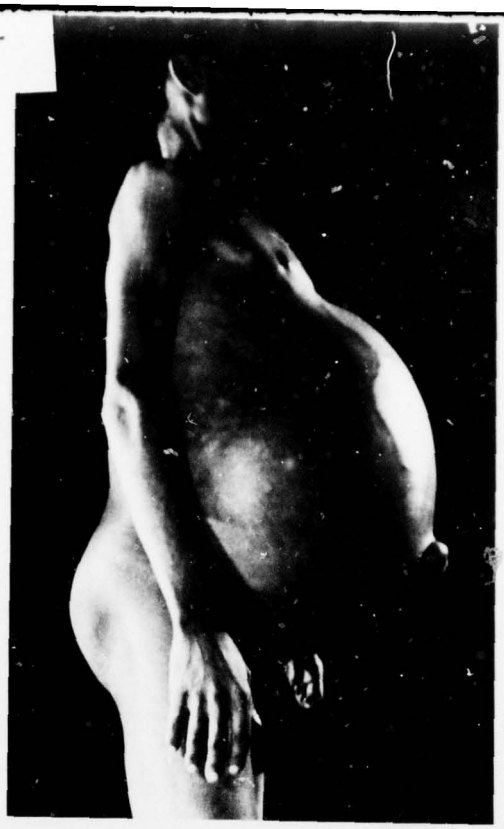


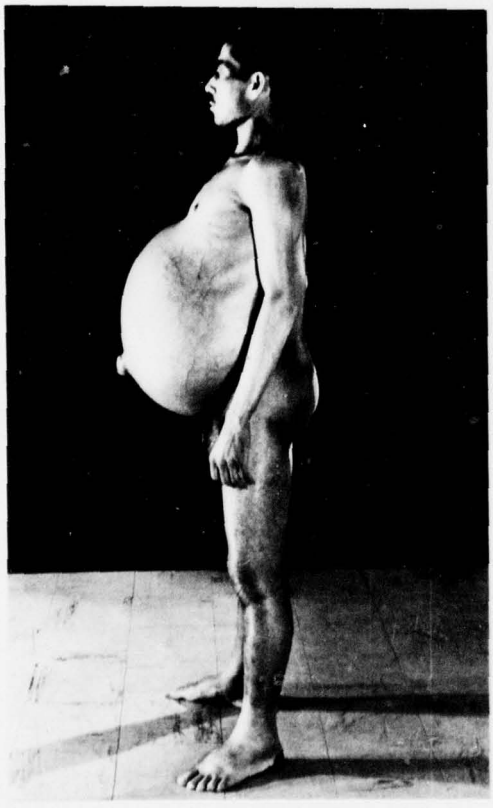


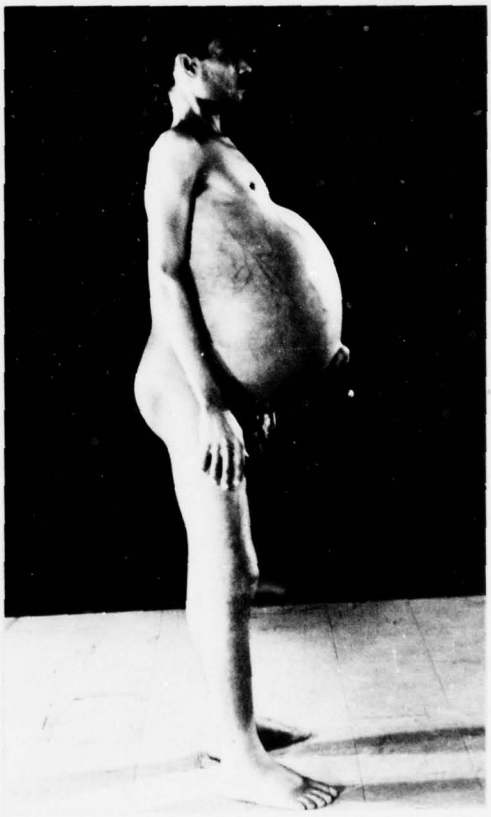


SAME PATIENT AS IN PAGE 2









AN ADULT PATIENT FROM PROJECT AREA, 30 YEARS OLD, WITH A) SCHISTO. HEPATOSPLENOMEGALY, B) MARKED ASCITES, C) PROTRUDED UMBILUCUS, D) SCROTAL OEDEMA, E) OEDEMA OF THE LOWER LIMBS AND F) PORTO-SYSTEMIC COLLATERALS.